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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/845,514	04/30/2001	K. Roger Aoki	D2929CON	3428

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EXAMINER

FORD, VANESSA L

ART UNIT	PAPER NUMBER
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1645

DATE MAILED: 08/29/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/845,514

Applicant(s)

AOKI ET AL.

Examiner

Vanessa L. Ford

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 13 June 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-9, 17-25 and 28-33 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-9, 17-25 and 28-33 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

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FINAL ACTION

1. This Office Action is responsive to Applicant's response filed June 13, 2005.
2. The text of those sections of Title 35, U.S. Code not included in this action can be found in the prior Office Action.

Rejection Maintained

3. The rejection under 35 U.S.C. 103(a) as unpatentable over Ludlow et al in view of Simpson and further in view of Jankovic et al is maintained for claims 1-9 for the reasons set forth ^{on} pages 3-5 paragraph 4 of the previous Office Action.

The rejection was on the grounds that Ludlow et al teach a composition comprising botulinum toxin type F used in the treatment of patients with torticollis and oromandibular dystonia after these patients have been treated with botulinum toxin A and they had developed antibodies to toxin A (page 350, col. 1)

Ludlow et al do not teach the other serotypes that are claimed.

Simpson et al teach the pharmacological structure and activity of each of the claimed serotypes, stating that there are all various strains of *C. botulinum* and are antigenically distinct and they all depress neurogenic release of acetylcholine (pages 155-156, 167 and 180).

Jankovic et al teach the use of botulinum toxin A to treat a number of neurological disorders. Jankovic et al teach that the toxin has the possibility of being blocked by antibodies and as such the treatment becomes ineffective after repeated injections of the toxins has anti-botulinum toxin antibodies developed (page 1189). Jankovic et al states that "it is likely that patients with antibodies against botulinum toxin will respond to injections with other botulinum toxins that are immunologically distinct from type A". Jankovic et al further teach that "any muscle spasm can be temporarily relieved by treatment with the toxin because botulinum toxin acts on the final common pathway".

It would be *prima facie* obvious at the time the invention was made to add botulinum toxin type F with botulinum toxin type A because the patients had developed antibodies to toxin A, Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct. Therefore, it would it would have

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been obvious to one of ordinary skill in the art to extend the teachings of Ludlow et al of administering toxin F after toxin A to other serotypes and to administer other serotypes after A as claimed with a reasonable expectation that serotypes other than type F will treat the types of neuromuscular disorders as demonstrated by Ludlow et al. It would be expected barring evidence to the contrary, that the combinations of serotypes of botulinum toxins would be effective in treating patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

Applicant urges that the claims are directed to a method in which a combination of two neurotoxins are administered simultaneously. Applicant urges that Ludlow et al teach the administration of botulinum toxin serotype F after the administration of botulinum toxin serotype A (patients have developed antibodies to serotype A).

Applicant urges that the combination of references do not teach, disclose or suggest the claimed invention. Applicant ~~urges~~ that the different serotypes are administered at different ~~times~~. Applicant urges that the prior art does not teach treating a patient suffering from a neuromuscular disorder wherein at least two neurotoxins are administered to the patient simultaneously.

Applicant's arguments filed June 13, 2005 have been fully considered but they are not persuasive. Ludlow et al as well as Jankovic et al provide that motivation for the combining more than one serotype of botulinum toxin in a composition to be administered to a subject which has a neuromuscular disorder because these prior art references teach that patients can develop antibodies to botulinum toxin serotypes after a long period of using a particular serotype for treatment. However, Simpson teaches that the serotypes are all common in their function and are immunologically distinct.

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Therefore, one of skill in the art would have been motivated to administer combinations of botulinum toxin serotypes to a patient suffering from a neuromuscular disorder because Ludlow et al teach that other serotypes (such as serotype F) are just as effective as serotype A in treating patients with neuromuscular disorders. One of ordinary skill in the art would expect a reasonable expectation of success when using a combination of botulinum toxin serotypes to treat patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

To address Applicant's comments regarding the teachings of the prior art references in regards to "simultaneous administration of different serotypes of botulinum toxin", it should be noted that the combination of the teachings of the prior art references must be considered. As stated above, the teachings of Ludlow et al and Jankovic et al provide that motivation for the combining more than one serotype of botulinum toxin in a composition to be administered to a subject which has a neuromuscular disorder and Simpson teach that all botulinum serotypes are all common in their function and are immunologically distinct. Therefore, one of ^{Ordinary} skill in the art would be motivated to use any combination of botulinum toxin serotypes since all Serotypes have the same function. It should be noted that MPEP 2144.06 teach that:

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It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) and In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

4. The rejection under 35 U.S.C. 103(a) as unpatentable over Ludlow et al in view of Simpson and further in view of Jankovic et al is maintained for claims 17-25 and 28-33 for the reasons set forth pages 5-7 paragraph 5 of the previous Office Action.

The rejection was on the grounds that Ludlow et al teach a composition comprising botulinum toxin type F used in the treatment of patients with torticollis and oromandibular dystonia after these patients have been treated with botulinum toxin A and they had developed antibodies to toxin A (page 350, col. 1)

Ludlow et al do not teach the other serotypes that are claimed.

Simpson et al teach the pharmacological structure and activity of each of the claimed serotypes, stating that there are all various strains of *C. botulinum* and are antigenically distinct and they all depress neurogenic release of acetylcholine (pages 155-156, 167 and 180).

Jankovic et al teach the use of botulinum toxin A to treat a number of neurological disorders. Jankovic et al teach that the toxin has the possibility of being blocked by antibodies and as such the treatment becomes ineffective after repeated injections of the toxins has anti-botulinum toxin antibodies developed (page 1189). Jankovic et al states that "it is likely that patients with antibodies against botulinum toxin will respond to injections with other botulinum toxins that are immunologically distinct from type A". Jankovic et al further teach that "any muscle spasm can be temporarily relieved by treatment with the toxin because botulinum toxin acts on the final common pathway".

It would be *prima facie* obvious at the time the invention was made to add botulinum toxin type F with botulinum toxin type A because the patients had developed

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antibodies to toxin A, Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct. Therefore, it would have been obvious to one of ordinary skill in the art to extend the teachings of Ludlow et al of administering toxin F after toxin A to other serotypes and to administer other serotypes after A as claimed with a reasonable expectation that serotypes other than type F will treat the types of neuromuscular disorders as demonstrated by Ludlow et al. It would be expected barring evidence to the contrary, that the combinations of serotypes of botulinum toxins would be effective in treating patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

Applicant urges that the combination of references do not teach, disclose or suggest the claimed invention. Applicant urges that a person of ordinary skill in the art would be required to guess, test, speculate and/or arbitrarily "pick and choose" two specific neurotoxins (e.g. botulinum toxin A and B or A and E) from the list of seven different serotypes identified by Simpson. Applicant urges that Simpson does not place any significance whatsoever in the types of botulinum toxin, let alone in a combination of botulinum toxin serotypes A and B or A and E, relative to the other botulinum toxin serotypes disclosed. Applicant urges that the general disclosure of Simpson alone or in combination with Ludlow et al or Jankovic et al do not teach the claimed compositions. Applicant urges that for example the combination of serotypes A and G is insufficient for Simpson alone or in combination with Ludlow et al or Janlovic et al.

Applicant's arguments filed June 13, 2005 have been fully considered but they are not persuasive. It is the Examiner's position that applicant argues the references individually without clearly addressing the combination of teachings. It is the

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combination of all of the cited and relied upon references which make up the state of the art with respect to the claimed invention. Ludlow et al as well as Jankovic et al provide that motivation for the combining more than one serotype of botulinum toxin in a composition to be administered to a subject which has a neuromuscular disorder because these prior art references teach that patients can develop antibodies to botulinum toxin serotypes after a long period of using a particular serotype for treatment. However, Simpson teaches that the serotypes are all common in their function and are immunologically distinct. Therefore, one of skill in the art would have been motivated to administer any combination of botulinum toxin serotypes to a patient suffering from a neuromuscular disorder because Ludlow et al suggests that other serotypes (such as serotype F) are just as effective as serotype A in treating patients with neuromuscular disorders. One of ordinary skill in the art would expect a reasonable expectation of success when using any combination of botulinum toxin serotypes to treat patients with neuromuscular disorders because Simpson teaches that the serotypes are all common in their function and are immunologically distinct and Jankovic et al suggest that patients who have developed antibodies to one toxin serotype will respond to injections of another serotype because they are all immunologically distinct.

To address Applicant's comments regarding for example administering to a patient the combination of serotype A and G, it should be noted that the combination of the teachings of the prior art references must be considered. As stated above, the teachings of Ludlow et al and Jankovic et al provide that motivation for the combining

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more than one serotype of botulinum toxin in a composition to be administered to a subject which has a neuromuscular disorder because of the development of antibodies to a particular serotype and Simpson teach that all botulinum serotypes are all common in their function and are immunologically distinct. Therefore, one of skill in the art would be motivated to use any combination of botulinum toxin serotypes since all serotypes have the same function. Thus, the combination of prior art teachings suggest that any combination of botulinum toxin serotypes would be sufficient for treating neuromuscular disorders.

To address Applicant's comments regarding arbitrarily picking and choosing combinations of botulinum serotypes, it should be noted that Simpson teach that all botulinum serotypes are all common in their function and are immunologically distinct.

It should be noted that MPEP 2144.06 teach that:

It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980) See also In re Crockett, 279 F.2d 274, 126 USPQ 186 (CCPA 1960) (Ex parte Quadranti, 25 USPQ2d 1071 (Bd. Pat. App. & Inter. 1992) and In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

There is nothing on the record to show that the combination of teachings would not suggest the claimed invention.

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5. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Conclusion


6. Any inquiry of the general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Office Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for the Group 1600 is (703) 872-9306.

Any inquiry concerning this communication from the examiner should be directed to Vanessa L. Ford, whose telephone number is (571) 272-0857. The examiner can normally be reached on Monday – Friday from 9:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Lynette Smith, can be reached at (571) 272-0864.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov/>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Vanessa L. Ford
Biotechnology Patent Examiner
August 17, 2005


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